

**REMARKS**

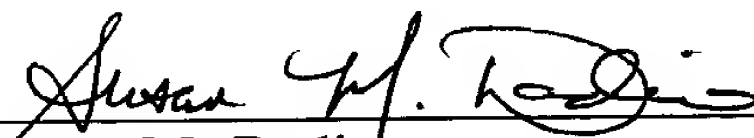
Entry of the foregoing and favorable consideration of the subject application, in light of the following remarks, are respectfully requested.

By the foregoing amendment, the specification has been amended to insert the sequence identifiers at the appropriate location throughout the specification. Moreover, the claims have been amended to eliminate the multiple dependencies in the claims and to place such claims in proper U.S. format. New new matter has been added by the present amendment.

In the event that there are any questions relating to this Preliminary Amendment, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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**Attachment to Preliminary Amendment dated April 24, 2000**

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**Page 11, Paragraph Beginning at Line 26**

The invention relates to a protein or a peptide capable of restoring the MHC II expression in cells from MHC II deficiency patients in complementation group B and comprising all or part of the amino acid sequence shown in figure 2 (SEQ ID NO: 11).

**Page 12, Paragraph Beginning at Line 12**

The invention relates to a protein or a peptide consisting or comprising the amino acid sequence shown in figure 2 (SEQ ID NO: 11) or an amino acid sequence having at least 80 %, 90 % and preferably at least 95 % identity or similarity with the amino acid sequence shown in figure 2 (SEQ ID NO: 11). The invention relates also to a protein or a peptide consisting or comprising the amino acid sequence of a functional part of the amino acid sequence shown in figure 2 (SEQ ID NO: 11) or of an amino acid sequence having at least 80 %, 90 % and preferably at least 95 % identity or similarity with a functional part of the amino acid sequence shown in figure 2 (SEQ ID NO: 11). The functional parts, homologous sequences and parts thereof are referred to as "derivatives".

**Page 12, Paragraph Beginning at Line 18**

The invention also relates to a functional part of the amino acid sequence shown in Figure 2 (SEQ ID NO: 11) free of the remainder of said amino acid sequence, optionally in association with an amino acid sequence different from said remainder.

**Page 13, Paragraph Beginning on Line 13**

A « functional part » is a part which has conserved the function of the protein having the amino acid sequence shown in figure 2 (SEQ ID NO: 11) (RFX-ANK).

**Page 13, Paragraph Beginning at Line 16**

The function of the protein having the amino acid sequence shown in figure 2 (SEQ ID NO: 11) (RFX-ANK) can be defined as the capacity to enable the functional transcription of MHC class II genes, via the RFX complex, and consequently the expression of MHC class II gene products.

**Page 13, Paragraph Beginning at Line 22**

A function of the protein having the amino acid sequence shown in figure 2 (SEQ ID NO: 11) (RFX-ANK) can be recognised as the capacity to correct the MHC II expression defect of cell lines from patients in complementation group B.

**Page 13, Paragraph Beginning at Line 26**

A function of the protein having the amino acid sequence shown in figure 2 (SEQ ID NO: 11) (RFX-ANK) is achieved globally by a series of sequential steps involved.

**Page 13, Paragraph Beginning at Line 30**

Thus, each of these steps can be considered, in the context of the invention, as being the direct or indirect function of the protein having the amino acid sequence shown in figure 2 (SEQ ID NO: 11) (RFX-ANK).

**Page 13, Paragraph Beginning at Line 34**

Consequently, a function of the protein having the amino acid sequence shown in figure 2 (SEQ ID NO: 11) (RFX-ANK) signifies the capacity to allow the expression of MHC class II molecules, to allow the transcription of an MHC class II gene, to allow the expression or the translation of an MHC class II protein or peptide, to allow the formation of the RFX complex, to allow the binding of the RFX complex to its DNA target (especially the X box motif), to allow the interaction between the RFX complex and at least one of the transcription factors X2BP, NF-Y or CIITA, to allow a cooperative interaction that stabilizes the higher order RFX-X2BP-NF-Y complex, to direct contacts between RFX and the co-activator CIITA, to allow binding of RFX5 to the X box, or to correct the MHC II expression defect of cell lines from patients in complementation group B.

**Page 14, Paragraph Beginning at Line 14**

In a preferred embodiment, a function of the protein having the amino acid sequence shown in figure 2 (SEQ ID NO: 11) (RFX-ANK) is to allow the interaction between the RFX complex and CIITA, to allow a cooperative interaction that stabilizes the higher order RFX-X2BP-NF-Y complex, to direct contacts between RFX and the co-activator CIITA or the recruitment of CIITA.

**Page 14, Paragraph Beginning at Line 21**

A « functional part » may not comprise some of the residues of the N-terminal domain of the amino acid sequence shown in figure 2 (SEQ ID NO: 11). In particular, a « functional part » may exclude the 65, 70, 80, 90, 91, 100, 110 first residues of the N-terminal region of the amino acid sequence shown in figure 2 (SEQ ID NO: 10).

**Page 14, Paragraph Beginning at Line 27**

The invention relates to a protein or a peptide comprising the amino acid sequence shown in figure 2 (SEQ ID NO: 11) and part thereof, or an amino acid sequence having at least 80 %, 90 % and preferably at least 95 % identity, similarity or homology with the illustrated sequences and part thereof. The homologous sequences and parts thereof are referred to as "derivatives".

**Page 15, Paragraph Beginning at Line 1**

The amino acid sequence shown in figure 2 (SEQ ID NO: 11) is the human sequence of RFX-ANK. Derivatives of the figure 2 (SEQ ID NO: 11) sequence may be agonists or antagonists of the RFX-ANK function as defined below.

**Page 16, Paragraph Beginning at Line 24**

The nucleic acid molecule of the invention may comprise all or part of the nucleotide sequence illustrated in figure 2 (SEQ ID NO: 10) (GenBank Accession Number: Human RFXANK cDNA AF094760).

**Page 17, Paragraph Beginning at Line 3**

In a further embodiment, the invention relates to a nucleic acid molecule comprising the nucleotide sequence illustrated in figure 2 (SEQ ID NO: 10) to a nucleotide sequence exhibiting at least 90 % identity with said nucleotide sequence or to a part of said nucleotide sequence.

**Page 19, Paragraph Beginning at Line 25**

The molecule of interest of the present invention is a protein, a peptide or a nucleic acid molecule of the invention encoding said protein or peptide. The molecule is called a transcription factor of the invention. The transcription factors may be RFX-ANK as shown in figure 2 (SEQ ID NO: 10) or derivatives thereof as described earlier.

**Page 33, Paragraph Beginning at Line 1**

Said product may particularly be a DNA molecule coding for RFXANK as it is shown in figure 2 (SEQ ID NO: 10), any DNA sequence with at least 80 % identity, preferably 90 % identity with said DNA molecule or any part of said DNA molecule or said DNA sequence.

**Page 45, Heading Beginning at Line 3**

**Figure 2 (SEQ ID NOS: 10 and 11): Sequence analyses of RFXANK.**

**Page 45, Paragraph Beginning at Line 14**

**--Figure 3 (SEQ ID NOS: 12, 13, 18 and 19): Sequences comparisons**

Amino acid sequence alignment between RFXANK and homologous proteins containing ankyrin repeats. The human RFXANK sequence is shown at the top (Hs RFXANK) (SEQ ID NO: 12). Identical amino acids in mouse RFXANK (Mm RFXANK) (SEQ ID NO: 13) and the other proteins are shown as dashes. Gaps are represented by points. 'Hs homol' (SEQ ID NO: 18) and 'Mm homol' (SEQ ID NO: 19) correspond to the predicted translation products of cDNAs encoding a highly homologous protein present in humans and mice, respectively. The ankyrin repeat-containing region of mouse GABPb (ref. 28) is shown at the bottom. The secondary structure prediction of the ankyrin repeats (ank 1-3) was inferred from the known structure of GABPb (ref. 35). H, helix; T, turn

**Page 46, Heading Beginning at Line 10**

**--Figure 5 (SEQ ID NOS: 14, 15, 16 AND 17):--**

**Page 55, Paragraph Beginning at Line 25**

Perfect matches to three independent peptides (Fig. 2a) (SEQ ID NO: 11) were identified in a variety of ESTs as well as in the theoretical protein product deduced from a gene identified by genomic DNA sequencing (GenBank accession number 2627294). The complete sequence of the corresponding mRNA (Fig. 2a) (SEQ ID NO: 10) was determined by assembling the ESTs into a single contig and by comparing it to the genomic sequence.

**Page 56, Paragraph Beginning at Line 18**

The resulting sequence was confirmed by comparison with the genomic sequence and by RT-PCR amplification and sequencing of RFXANK cDNA clones from control B cell lines (Raji and QBL). The following primers were used to amplify RFXANK cDNAs by PCR: 5'p33 (5'- CCGTACGCGTCTAGACCATGGAGCTTACCCAGCCTGCAGA-3') (SEQ ID NO: 1), which overlaps the translation initiation codon, and 3'p33 (5'- TTCGAATTCTCGAGTGTCTGAGTCCCCGGCA-3') (SEQ ID NO: 2), which is complementary to the 3' untranslated region of RFXANK mRNA. Homology to RFXANK mRNA is underlined. The primers contain restriction sites at their 5' ends to facilitate cloning. RFXANK cDNAs were cloned into the expression plasmid EBO-76PL (ref.<sup>8</sup>) and



pBluescript KS (Stratagene). 12 RFXANK cDNA clones were sequenced on both strands. The nucleotide and amino acid sequences of human RFXANK were tested for homology to sequences in EMBL, GenBank, SwissProt, and dbEST. Sequence analysis was performed with PC/gene (Intelligenetics), BLAST programs available through the NCBI server (<http://www.ncbi.nlm.nih.gov>), and a variety of proteomics tools (<http://www.expasy.ch/www/tools.html>). For multiple protein sequence alignments, CLUSTALW (<http://www2.ebi.ac.uk/clustalw>) was used. ESTs were assembled into contigs with the TIGR Assembler (<http://www.tigr.org>). The search for homology to human RFXANK identified EST clones corresponding to mouse (AA435121, AA616119, AA259432, AA146531) and rat (AA851701) orthologs, and to a highly homologous gene present in both man (AA496038, AA442702, AA205305, N25678, N70046, AA418029, AA633452, H39858, R86213, AA418089, N64316, R63682, N55216) and mouse (AA245178, Z31339, AA118335). The sequences of mouse Rfxank and of the human and mouse homologues were determined by organizing the corresponding ESTs into contigs. The mouse Rfxank sequence was confirmed by amplifying the cDNA by RT-PCR from C57BL6 mouse spleen RNA using the following primers :

m5'p33 (5'- CCGTACGCGTCTAGACCATGGAGCCCACTCAGGTTGC -3') (SEQ ID NO: 3), which overlaps the translation initiation codon, and m3'p33 (5'- TTCGAATTCTCGAGTGCCTGGGTTCCAGCAGG -3') (SEQ ID NO: 4), which is complementary to the 3' untranslated region of Rfxank mRNA. Homology to mouse Rfxank mRNA is underlined. The primers included 5' extensions with restriction sites that

were used to clone the mouse Rfxank cDNA directly into the EBO-76PL expression vector<sup>8</sup>. 14 clones were sequenced on both strands.

**Page 57, Paragraph Beginning at Line 23**

Two splice variants were identified at approximately equal frequencies. They differ only by the insertion of a single CAG triplet (Fig. 2a) (SEQ ID NO: 10) and probably result from the alternative usage of two possible splice acceptor sites situated 3 nucleotides apart upstream of exon 4. An additional minor splice variant lacking exon 5 (see Fig. 2a) (SEQ ID NO: 10) was also identified, both in an EST and in one of the cDNA clones (data not shown).

**Page 57, Paragraph Beginning at Line 32**

The cDNA corresponding to the 33 kDa protein contains a 260 amino acid open reading frame. The translation initiation codon is preceded by an in-frame TGA stop codon, indicating that the coding region is complete. The deduced molecular weight (28.1 kDa) and isoelectric point (4.45) correspond well to the biochemical parameters determined for p33 in one- and two-dimensional gel electrophoresis (data not shown). The protein encoded by the open reading frame is novel. In particular, it exhibits no homology to either RFXAP or RFX5, the two other known subunits of the RFX complex, nor to other members of the RFX family of DNA binding proteins<sup>24</sup>. A search for homology to known proteins and motifs did identify the presence of three ankyrin repeats (Fig. 2b) (SEQ ID

NO: 11). Together with the fact that it is an essential subunit of the RFX complex, this led us to call the protein RFXANK. Outside of the ankyrin repeat region, the only other recognizable feature is an N-terminal acidic region resembling transcription activation domains.

**Page 58, Paragraph Beginning at Line 16**

EST clones corresponding to mouse and rat Rfxank were also identified in the data base. Mouse ESTs were organized into a contig to generate a partial mouse sequence, which was then confirmed and completed by isolating mouse Rfxank cDNA clones by RT-PCR. Homology to human RFXANK is high (85 % overall amino acid identity), particularly within and surrounding the ankyrin repeat region (94% amino acid identity, Fig. 2b) (SEQ ID NO: 11). Two different splice variants were found among mouse Rfxank cDNA clones. The major one, which is shown as the deduced amino acid sequence aligned with the human sequence in Fig. 2b (SEQ ID NO: 10), is characterized by an additional stretch of 10 amino acids that precedes the first ankyrin repeat. A minor splice variant lacking these additional 10 amino acids was also represented among the mouse cDNA clones isolated (not shown). RFXANK may belong to a family of related proteins because we identified a number of additional EST clones corresponding to at least one human and one mouse gene exhibiting a high degree of homology to RFXANK gene (Fig 2b) (SEQ ID NO: 10). These are by far the most closely related sequences currently present in the data base. In addition, the ankyrin repeats of RFXANK show distinct but

more limited homology (25-40% identity) to ankyrin repeat regions of a variety of other proteins<sup>20,21</sup>, including the b subunit of the transcription factor GABP (ref. <sup>28,29</sup>, see Fig. 2b) (SEQ ID NO: 10).

**Page 60, Paragraph Beginning at Line 33**

The entire coding region of RFXANK mRNA was amplified by RT-PCR from patient cells using the 5'p33 and 3'p33 primers described above. PCR products were subcloned into pBluescript and sequenced on both strands. For each patient, 3 independent cDNA clones were sequenced. The genomic DNA spanning exons 4 to 7 was amplified by PCR from patient cells using an exon 4 specific primer (5'-CCAGCTCTAGACTCCACCACTCTCACCAAC-3') (SEQ ID NO: 5) having a 5' extension containing an XbaI site (underlined) and an exon 7 specific primer (5'-CCTTCGAATTCTCGCTCTTTTGCCAGGATG-3') (SEQ ID NO: 6) having a 5' extension containing an EcoRI site. PCR products were subcloned into pBluescript KS (Stratagene) and 6 independent subclones were sequenced for each patient. Analysis of the wild type and deleted alleles in the patients and their families was done by PCR using intronic primers flanking exon 6; (5'-GGTTCTCTAGATTGGCAGCACTGGGGATAG-3') (SEQ ID NO: 7) and (5'-GCTACGAATTCCAGCAGACACAGCCAAAAC-3') (SEQ ID NO: 8). These primers carry 5' extensions containing, respectively, XbaI and EcoRI sites (underlined). The sizes of the wild type and deleted PCR products are, respectively, 265 bp, 239 bp (Ab and Na) and 207 bp (BLS1).

**Page 61, Paragraph Beginning at Line 22**

Analysis of several independent cDNA clones revealed the presence in all three patients of the same aberrant form of RFXANK mRNA lacking exons 5 and 6 (Fig. 4a). Splicing of exon 4 to exon 7 leads to a frame shift followed by an out of frame stop codon (Fig. 4a) and thus results in the synthesis of a severely truncated RFXANK protein lacking the entire ankyrin repeat region (see Fig. 2b) (SEQ ID NO: 10).

**Page 62, Paragraph Beginning at Line 30**

In vitro transcription-translation reactions and electrophoretic mobility shift assays (EMSA) using nuclear extracts and in vitro translated proteins were done as described<sup>9,22,50</sup>. The production of polyclonal rabbit antisera specific for RFX5 and RFXAP and their use in supershift experiments have also been described<sup>10</sup>. The monoclonal anti-FLAG antibody (M2, Kodak) was used in supershift experiments at a final concentration of 20 ng/ml. The RFXANK cDNA tagged with a FLAG epitope at its N terminus was constructed as follows: The entire RFXANK open reading frame was amplified from pEBO-RFXANK plasmid by PCR with primers 3'p33 (described above) and FLAG-5'p33 (5'-CCGTACGCGTCTAGAATGGATTACAAAGACGATGACGATAAGATGGAGCTTACCCAGCCTGCAGAAGAC -3') (SEQ ID NO: 9). The FLAG epitope (DYKDDDDK) coding sequence is underlined. The PCR product containing the FLAG sequence fused to the 5' end of RFXANK was cloned in pBluescript KS (Stratagene).

**Attachment to Preliminary Amendment dated April 24, 2001**

**Marked-up Claims 1-61**

1. (Amended) [Protein] A protein or peptide capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in figure 2.
2. (Amended) [Protein] The protein or peptide according to claim 1 wherein the cells are BLS 1 cell line, [or] Na cell line or Ba cell line.
3. (Amended) [Protein] The protein or peptide according to claim 1 [or 2] wherein the MHC-II is HLA-DR, [or] HLA-DP or HLA-DQ.
4. (Amended) [Protein] A protein or peptide [consisting or] comprising the amino acid sequence shown in figure 2[, an amino acid sequence having at least 80 % or preferably at least 90 % identity or similarity with the amino acid sequence shown in figure 2, a functional part of the amino acid sequence shown in figure 2 or a functional part of an amino acid sequence having at least 80 % and preferably at least 90 % homology with the amino acid sequence shown in figure 2].

5. (Amended) [Protein] A protein or peptide which is the homologous protein of a protein or a peptide of [any one of claims] claim 1 [to 4] in another species than human.

6. (Amended) [Protein] The protein or peptide of claim 5 wherein the species is pig.

7. (Amended) Antibodies capable of specifically [recognising] recognizing a peptide or protein according to [any of] claim 1 [to 6].

8. (Amended) [Antibodies] The antibodies according to claim 7 [which] wherein said antibodies are monoclonal.

9. (Amended) [Antibodies] The antibodies according to [claims] claim 7 [or 8 which] wherein said antibodies are single chain antibodies.

10. (Amended) [Antibodies] The antibodies according to [anyone of claims] claim 7 [to 9 which] wherein said antibodies are capable of inhibiting a function or an activity of [a] said protein or a peptide [of any one of claims 1 to 6].

11. (Amended) [Nucleic] A nucleic acid molecule encoding a protein or a peptide according to [any one of claims] claim 1 [to 6 or a chain of antibodies according to any one of claim 7 to 10].

12. (Amended) [Nucleic] The nucleic acid molecule according to claim 11 comprising all or part of the nucleotide sequence illustrated in figure 2.

13. (Amended) [Nucleic] A nucleic acid molecule comprising a sequence complementary to the nucleic acid [molecules] molecule of [any one of claims] claim 11 [to 12].

14. (Amended) [Nucleic] A nucleic acid molecule capable of hybridizing in stringent conditions, with the nucleic acid [molecules] molecule of [any one of claims] claim 11 [to 13].

15. (Amended) [Nucleic] A nucleic acid molecule comprising at least one of the sequences illustrated in figures 2[, or a sequence exhibiting at least 90 % identity or similarity with any of these sequences, or a functional part of any one of these sequences].



16. (Amended) [Nucleic] The nucleic acid molecule of [anyone of claims] claim 11 [to 15 comprises] comprising all or part of the DNA molecule encoding the RFXANK gene of a species other than human.

17. (Amended) [Nucleic] The nucleic acid molecule of claim 16 wherein the species is pig.

18. (Amended) [Nucleic] A nucleic acid molecule comprising a sequence complementary to the nucleic acid molecule of [anyone of claims] claim [11, 12 or] 14 [to 17].

19. (Amended) [Anti-sense] An anti-sense molecule or ribozyme comprising [a] the nucleic acid molecule of claim 13 [or 18].

20. (Amended) [Vector] A vector comprising [a] the nucleic acid molecule of [any one of claims] claim 11 [to 19].

21. (Amended) [Process] A process for identifying inhibitors which have the capacity to inhibit a function or an activity of a protein or a peptide according to [any one of claims] claim 1 [to 6 or of a nucleic acid molecule according to any one of claims 11 to

18] comprising detecting or measuring of said function or activity after intervention of the potential inhibitor.

22. (Amended) [Process] The process according to claim 21 wherein said function or activity is the expression of MHC class II molecules.

23. (Amended) [Process] The process according to claim 22 wherein the expression of MHC class II molecules is measured at the surface of cells.

24. (Amended) [Process] The process according to claim 22 wherein the expression of MHC class II is measured at the mRNA level or in the cells.

25. (Amended) [Process] The process according to claim 23 [or 24] wherein said cells are B lymphocyte cell lines with constitutive expression of MHC class II or interferon gamma inducible cell lines.

26. (Amended) [Process] The process according to claim 21 wherein said function or activity is the formation of RFX complex.

27. (Amended) [Process] The process according to claim 21 wherein said function or activity is the binding of the RFX complex to its DNA target.

28. (Amended) [Process] The process according to claim 27 wherein the measure or detection of the function or activity is done by gel retardation assay.

29. (Amended) [Process] The process according to claim 21, wherein said function or activity is the interaction between the RFX complex and at least one of transcription factors X2BP, NF-Y and CIITA.

30. (Amended) [Process] The process according to claim 21 wherein said function or activity is the correction of the MHC II expression defect of cell lines from complementation group B.

31. (Amended) [Process] A process for identifying inhibitors which have the capacity to inhibit the synthesis of a protein or a peptide according to [any one of claims] claim 1 [to 6 or of a nucleic acid molecule according to any one of claims 11 to 18] comprising detection or measuring a product which contributes to the synthesis of said protein or peptide after intervention of the potential inhibitor.

32. (Amended) [Process] The process according to claim 31 wherein said product is mRNA.

33. (Amended) [Process] The process according to [any one of claims] claim 21 [to 32] comprising a preliminary screening of said potential [inhibitor which consists in screening for the binding of molecules to a peptide or a protein of any one of claims 1 to 6 or nucleic acid molecule of any one of claims 11 to 18] inhibitors.

34. (Amended) [Process] A process of screening which [consists in] comprises screening for the binding of molecules to [a] the peptide or a protein of [any one of claims] claim 1 [to 6] or a part thereof [or which consists in screening for the binding of molecules to nucleic acid molecule of any one of claims 11 to 18 or a part thereof].

35. (Amended) [Process] The process according to claim [33 or] 34 wherein the binding of molecules is detected by ligand-induced charge in protein conformation.

36. (Amended) [Process] The process according to claim [33 or] 34 wherein the binding of molecules is detected by ligand-induced displacement of molecules first identified as binding to a peptide or a protein of [any of claims 1 to 6] capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in figure 2.

37. (Amended) [Process] A process for identifying inhibitors which have the capacity to inhibit a function, an activity or the synthesis of a protein or a peptide

[according to any one of claims claim 1 to 6 or of a nucleic acid molecule according to any one of claims 11 to 18] capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in figure 2 comprising the designing of said inhibitors on the basis of the three dimensional structure of a protein or a peptide according to [any one of claims] claim 1 [to 6].

38. (Amended) [Process] The process according to claim 37 wherein the three dimensional structure is obtained using X-Ray structure analysis or spectroscopic methods.

39. (Amended) [Process] A process for identifying an inhibitor which has the capacity to inhibit recruitment of CIITA or to inhibit the binding or fixation of CIITA to the MHC-class II enhanceosome, said process comprising the following steps:

a DNA fragment consisting or comprising the W-X-X2-Y box region of the MHC II promoters is contacted with a mixture of cellular proteins comprising proteins binding to the W-X-X2-Y box region and CIITA, and with the substance to be tested;

the thus formed DNA-protein complex is separated from the reaction mixture;

the presence or absence of CIITA in the proteins obtained after step ii) is detected, absence of CIITA indicating that the substance under test has a capacity to inhibit CIITA recruitment.

40. (Amended) [Process] The process according to claim 39, wherein the DNA-protein complex is separated by fixation to a solid support able to purify said DNA-protein complex.

41. (Amended) [Process] The process according to claim 40, wherein a solid support comprises magnetic beads or a microtitration plate.

42. (Amended) [Process] The process according to [any one of] claim 41, wherein a DNA fragment consisting or comprising the W-X-X2-Y box region of the MHC II promoters is biotinylated.

43. (Amended) [Process] The process according to [any one of claim] claim 39 [to 42], wherein one or several wash(es) are carried out between step (ii) and step (iii) and/or wherein proteins binding DNA are separated from the DNA carried out between step (ii) and step (iii).

44. (Amended) [Process] The process according to [any one of claim] claim 39 [to 43], wherein the presence of CIITA in the proteins obtained after step iii) is detected by antibodies specific of CIITA.

45. (Amended) [Process] The process according to [any one of claim] claim 39 [to 44], wherein CIITA is chosen among: a recombinant or recombinantly produced, a mutant CIITA, a mutant CIITA which has greater affinity for the MHC-class II enhanceosome than a wild-type CIITA, a truncated version of a wild-type CIITA.

46. (Amended) [Process] The process according to [any one of claims] claim 39 [to 45], wherein CIITA is tagged or wherein CIITA comprises a Fluorescent Protein or an epitope.

47. (Amended) [Process] The process according to [any one of claims] claim 39 [to 46], wherein the substances to be tested are CIITA dominant negative mutants.

48. (Amended) [Process] The process according to [any one of claims] claim 39 [to 47], wherein the mixture of cellular proteins and CIITA comprises a nuclear extract of CIITA+ cells.

49. (Amended) [Process] The process according to [any one of claims] claim 39 [to 48] further comprising a step of separating the proteins bound to the DNA from the DNA and optionally detecting the presence or absence of any of the proteins capable of binding to the W-X-X2-Y region of the MHC-class II promoters, the absence of any of

these proteins indicating that the substance under test is capable of inhibiting the binding of said protein to DNA.

50. (Amended) [Inhibitor] An inhibitor identifiable by a process according to [any one of claims] claim 21 [to 49].

51. (Amended) [Inhibitor] The inhibitor according to claim 50 which is an antibody capable of specifically recognizing a protein or peptide capable of restoring the MHC-II expression in cells from MHC-II deficiency patients in complementation group B and comprising all or part of the amino-acid sequence shown in figure 2 [according to any one of claims 7 to 8, a nucleic acid molecule according to claim 13 or 18 a derivative of a protein or a peptide according to any one of claims 1 to 6 or of a nucleic acid molecule according to any one of claims 11 to 18, or an anti-sense molecule or a ribozyme according to claim 19].

52. (Amended) [Inhibitor] The inhibitor according to claim 50 which is an antibody, a single chain antibody, a dominant negative mutant, a protein, a peptide, a small molecular weight molecule, a ribozyme or an anti-sense molecule.



53. (Amended) Inhibitors of a protein or a peptide according to [any one of claims] claim 1 [to 6, or of a nucleic acid molecule according to any one of claims 11 to 18].

54. (Amended) [Nucleic] A nucleic acid molecule encoding an inhibitor of [any one of claims] claim 50 [to 53].

55. (Amended) [Inhibitor] A method of using the inhibitor according to [any one of claims] claim 50 [to 54 for use] in therapy comprising administering said inhibitor to a patient in need of said therapy.

56. (Amended) [Pharmaceutical] A pharmaceutical composition comprising an inhibitor according to [any one of claims] claim 50 [to 54, optionally] in association with a pharmaceutically acceptable vehicle.

57. (Amended) [Use of] A method of using an inhibitor according to [any one of claims] claim 50 [to 54] for the preparation of a medicament for use in therapy or prevention of diseases associated with aberrant expression of MHC class II genes.

58. (Amended) [Use of] A method of using an inhibitor according to [any one of claims] claim 50 [to 54] as an immunosuppressive agent comprising administering said inhibitor to a patient in need of said immunosuppressive agent.

59. (Amended) [Protein] A protein complex comprising cellular proteins capable of binding to the W-X-X2-Y box of MHC-class II promoters and CIITA.

60. (Amended) [Protein] The complex according to claim 59 wherein CIITA is : a recombinant or recombinantly produced CIITA, a mutant CIITA, a mutant CIITA which has greater affinity for the MHC-class II enhanceosome than a wild-type CIITA or a truncated version of a wild-type CIITA.

61. (Amended) Antibodies capable of specifically recognizing a protein complex according to [claims] claim 59 [and 60].